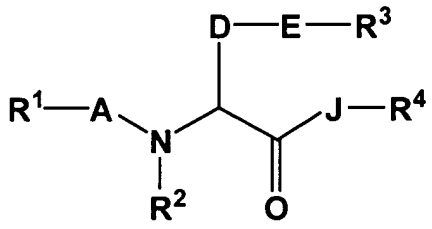
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (Currently Amended) An amino acid compound of the formula (I)



(I)

wherein,

R^1 is ~~a hetrocyclic ring~~ thiazolidinyl, oxazolidinyl or pyrrolidinyl which is substituted with (a) four C1-4 alkyl or (b) one substituent selected from the following (i)-(xii), and ~~the said ring~~ which may be substituted with 1 to 3 of substituent(s) selected from the group consisting of (i)-(xxiii):

(i) oxo,

(ii) C5-8 alkyl,

(iii) -COO-R^5 (in which, R^5 is hydrogen, C5-8 alkyl, C2-8 alkenyl, or C1-4 alkyl substituted with 1 to 3 of halogen or C1-4 alkoxy),

(iv) -(C1-4 alkylene)-COOR^6 (in which, R^6 is hydrogen, C1-8 alkyl, C2-8 alkenyl or C1-4 alkyl substituted with 1 to 3 of halogen),

(v) -CO-R^7 (in which, R^7 is C5-8 alkyl, C2-4 alkenyl, carbocyclic ring, heterocyclic ring or C1-8 alkyl substituted with one substituent selected from the following (1)-(8):

(1) carbocyclic ring,

(2) heterocyclic ring,

(3) hydroxy,

(4) C1-4 alkoxy,

(5) -OCO-(C1-4 alkyl),

(6) -O-(C1-4 alkylene)-O-(C1-4 alkyl),

(7) NR^8R^9 (in which, R^8 and R^9 each, independently, is hydrogen or C1-4 alkyl),

(8) halogen),

(vi) -(C1-4 alkylene)-CO-R^{10} (in which, R^{10} is C1-8 alkyl, C2-4 alkenyl, carbocyclic ring, heterocyclic ring or C1-8 alkyl substituted with one substituent selected from the following (1)-(8):

(1) carbocyclic ring,

(2) heterocyclic ring,

(3) hydroxy,

(4) C1-4 alkoxy,

(5) -OCO-(C1-4 alkyl),

(6) -O-(C1-4 alkylene)-O-(C1-4 alkyl),

(7) $NR^{11}R^{12}$ (in which, R^{11} and R^{12} each, independently, is hydrogen or C1-4 alkyl),

(8) halogen),

(vii) -CO-CO-R^{13},

(viii) -CO-(C1-4 alkylene)-CO-R^{14},

(ix) $-SO_2-R^{15}$ (in which, R^{13}, R^{14} and R^{15} each, independently, is C1-8 alkyl, C2-4 alkenyl, carbocyclic ring, heterocyclic ring, hydroxy, C1-4 alkoxy or C1-8 alkyl substituted with one substituent selected from the following (1)-(8):

(1) carbocyclic ring,

(2) heterocyclic ring,

(3) hydroxy,

(4) C1-4 alkoxy,

(5) -OCO-(C1-4 alkyl),

(6) -O-(C1-4 alkylene)-O-(C1-4 alkyl),

(7) $NR^{16}R^{17}$ (in which, R^{16} and R^{17} each, independently, is hydrogen or C1-4 alkyl),

(8) halogen),

(x) $-CONR^{18}R^{19}$ (in which, R^{18} is hydrogen or C1-4 alkyl which may be substituted with one phenyl, R^{19} is C1-8 alkyl or C2-4 alkenyl),

(xi) C1-8 alkyl substituted with 1 to 2 of substituent(s) selected from the group consisting of the following (1)-(7):

(1) hydroxy,

(2) C1-4 alkoxy,

(3) -O-(C1-4 alkylene)-O-(C1-4 alkyl),

(4) tetrahydropyran-2-yloxy,

(5) $-SR^{20}$ (in which, R^{20} is hydrogen or C1-4 alkyl),

(6) halogen,

(7) $NR^{21}R^{22}$ (in which, R^{21} and R^{22} each, independently, is hydrogen or C1-4 alkyl),

(xii) hydroxy,

(xiii) C1-4 alkyl,

(xiv) C1-4 alkoxy,

(xv) phenyl,

(xvi) phenoxy,

(xvii) benzyloxy,

(xviii) $-SR^{23}$ (in which, R^{23} is hydrogen or C1-4 alkyl),

(xix) C2-5 acyl,

(xx) halogen,

(xxi) C1-4 alkoxycarbonyl,

(xxii) nitro,

(xxiii) $-NR^{24}R^{25}$ (in which, R^{24} and R^{25} each, independently, is hydrogen, C1-4 alkyl or C1-4 alkoxycarbonyl, or R^{24} and R^{25} taken together with nitrogen atom to which is attached represents 5 to 7-membered saturated heterocyclic ring necessary containing one nitrogen atom and optionally further containing one nitrogen atom or one oxygen atom),

A is single bond, -CO- or $-SO_2-$,

R^2 is hydrogen or C1-4 alkyl which may be substituted with one phenyl,

D is C1-4 alkylene or C2-4 alkenylene,

E is

1) -COO-,

2) -OCO-,

3) -$CONR^{26}$- (in which, R^{26} is hydrogen or C1-4 alkyl),

4) -$NR^{27}CO$- (in which, R^{27} is hydrogen or C1-4 alkyl),

5) -O-,

6) -S-,

7) -SO-,

8) -SO_2-,

9) -NR^{28}- (in which, R^{28} is hydrogen or C1-4 alkyl),

10) -CO-,

11) -SO_2NR^{29}- (in which, R^{29} is hydrogen or C1-4 alkyl) or

12) -$NR^{30}SO_2$- (in which, R^{30} is hydrogen or C1-4 alkyl),

R^3 is

~~1) carbocyclic ring,~~

~~2) C1-4 alkyl substituted with carbocyclic ring or heterocyclic ring,~~

~~in which, all the said carbocyclic ring and heterocyclic ring in R^3~~

cyclopentylmethyl or cyclohexylmethyl which may be substituted with 1 to 3 of substituent(s) selected from the group consisting of the following (i)-(xi):

(i) C1-4 alkyl,

(ii) C1-4 alkoxy,

(iii) phenyl,

(iv) phenoxy,

(v) benzyloxy,

(vi) -SR^{31} (in which, R^{31} is hydrogen or C1-4 alkyl),

(vii) C2-5 acyl,

(viii) halogen,

(ix) C1-4 alkoxycarbonyl,

(x) nitro,

(xi) -$NR^{32}R^{33}$ (in which, R^{32} and R^{33} each, independently, is hydrogen, C1-4 alkyl or C1-4 alkoxycarbonyl, or R^{32} and R^{33} taken together with nitrogen atom to which is attached represents 5 to 7-membered saturated heterocyclic ring necessary containing one nitrogen atom and optionally further containing one nitrogen atom or one oxygen atom),

J is

1) -O-,

2) -NR^{34}- (in which, R^{34} is hydrogen, C1-4 alkyl which may be substituted with one phenyl, $NR^{35}R^{36}$ (in which, R^{35} and R^{36} each, independently, is hydrogen or C1-4 alkyl), hydroxy, C1-4 alkoxy, -(C1-4 alkylene)-OH, -(C1-4 alkylene)-O-(C1-4 alkyl) or -(C1-4 alkylene)-O-(C2-5 acyl)),

3) -NR^{37}-NR^{38}- (in which, R^{37} and R^{38} each, independently, is hydrogen or C1-4 alkyl which may be substituted with one phenyl),

4) -NR^{39}-(C1-4 alkylene)-NR^{40}- (in which, R^{39} and R^{40} each, independently, is hydrogen or C1-4 alkyl which may be substituted with one phenyl),

5) -NR^{41}-(C1-4 alkylene)-O- (in which, R^{41} is hydrogen or C1-4 alkyl which may be substituted with one phenyl) or

6) -NR^{42}-(C1-4 alkylene)-S- (in which, R^{42} is hydrogen or C1-4 alkyl which may be substituted with one phenyl),

R^4 is R^{4-1} or R^{4-2},

R^{4-1} is ~~a heterocyclic ring~~

~~or when J is $-NR^{34}-$, $-NR^{37}-NR^{38}-$ or $-NR^{39}-$(C1-4 alkylene)$-NR^{40}-$, each R^{4-1} and R^{34}, R^{4-1} and R^{38}, and R^{4-1} and R^{40}, taken together with the nitrogen atom to which they are attached, may represent a heterocyclic ring,~~

~~in which all the said heterocyclic ring in R^{4-1}, and heterocyclic ring represented by each R^{4-1} and R^{34}, R^{4-1} and R^{38}, and R^{4-1} and R^{40} taken together with nitrogen atom to which is attached~~ piperidinyl which may be substituted with 1 to 3 of substituent(s) selected from the group consisting of the following (i)-(x):

(i) C1-4 alkyl,

(ii) C1-4 alkoxy,

(iii) -SR^{46} (in which, R^{46} is hydrogen or C1-4 alkyl),

(iv) C2-5 acyl,

(v) halogen,

(vi) C1-4 alkoxycarbonyl,

(vii) nitro,

(viii) -$NR^{47}R^{48}$ (in which, R^{47} and R^{48} each, independently, is hydrogen, C1-4 alkyl or C1-4 alkoxycarbonyl),

(ix) hydroxy,

(x) -(C1-4 alkylene)-O-(C1-4 alkyl),

R^{4-2} is -L-M,

-L- is a ~~heterocyclic~~ piperidine ring,

~~or when J is $-NR^{34}-$, $-NR^{37}-NR^{38}-$ or $-NR^{39}-$(C1-4 alkylene)$-NR^{40}-$, each L and R^{34}, L and R^{38}, and L and R^{40}, taken together with the nitrogen atom to which they are attached, may represent a heterocyclic ring,~~

M is

1) carbocyclic ring,

2) heterocyclic ring,

3) C1-4 alkyl substituted with 1 to 2 of substituent(s) selected from the group consisting of the following (i)-(ii):

(i) carbocyclic ring,

(ii) heterocyclic ring,

4) -O-(carbocyclic ring or heterocyclic ring),

5) -S-(carbocyclic ring or heterocyclic ring),

6) $-NR^{49}-$(carbocyclic ring or heterocyclic ring) (in which, R^{49} is hydrogen or C1-4 alkyl which may be substituted with one phenyl),

7) -O-(C1-4 alkylene)-(carbocyclic ring or heterocyclic ring),

8) -S-(C1-4 alkylene)-(carbocyclic ring or heterocyclic ring),

9) $-NR^{50}-$(C1-4 alkylene)-(carbocyclic ring or heterocyclic ring) (in which, R^{50} is hydrogen, C1-4 alkyl which may be substituted with one phenyl or C2-5 acyl which may be substituted with 1 to 3 of halogen) or

10) -CO-(carbocyclic ring or heterocyclic ring),

or the said piperidine ring in L, and the said carbocyclic ring and heterocyclic ring in ~~L~~ ~~and~~ M~~, and heterocyclic ring represented by each L and R^{34}, L and R^{38}, and L and R^{40} taken together with nitrogen atom to which is attached~~ may be substituted with 1 to 3 of substituent(s) selected from the group consisting of the following (i)-(xiv):

(i) C1-4 alkyl,

(ii) C2-4 alkenyl,

(iii) hydroxy,

(iv) C1-4 alkoxy,

(v) -(C1-4 alkylene)-OH,

(vi) -(C1-4 alkylene)-O-(C1-4 alkyl),

(vii) halogen,

(viii) $NR^{51}R^{52}$ (in which, R^{51} and R^{52} each, independently, is hydrogen, C1-4 alkyl or C1-4 alkoxycarbonyl, or R^{51} and R^{52} taken together with nitrogen atom to which is attached represents 5 to 7-membered saturated heterocyclic ring necessary containing one nitrogen atom and optionally further containing one nitrogen atom or one oxygen atom),

(ix) SR^{53} (in which, R^{53} is hydrogen or C1-4 alkyl),

(x) nitro,

(xi) trifluoromethyl,

(xii) C1-4 alkoxycarbonyl,

(xiii) oxo,

(xiv) C2-5 acyl

or a non-toxic salt thereof, or a hydrate thereof.

2. (Original) A compound according to claim 1, in which E is -COO-, -O-, -S-, -SO- or $-SO_2-$.

3. (Original) A compound according to claim 1, in which E is -O- or -S-.

4.-9. (Canceled)

10. (Previously Amended) A compound according to claim 1 which is:

1) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(pyridin-3-ylcarbonyl)thiazolidin-4-ylcarbonylamino)propanamide,

2) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-acetyloxymethylcarbonylthiazolidin-4-ylcarbonylamino)propanamide,

3) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(2-methoxyacetyl)thiazolidin-4-ylcarbonylamino)propanamide,

4) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-allyloxycarbonylthiazolidin-4-ylcarbonylamino)propanamide,

5) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((4R)-3-(2-ethoxy-1,2-dioxoethyl)thiazolidin-4-ylcarbonylamino)propanamide,

6) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((4R)-3-phenylsulfonylthiazolidin-4-ylcarbonylamino)propanamide,

7) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-dimethylaminomethylcarbonylthiazolidin-4-ylcarbonylamino)propanamide,

8) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(morpholin-4-ylmethylcarbonyl)thiazolidin-4-ylcarbonylamino)propanamide,

9) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(3-hydroxy-3-methylbutyryl)thiazolidin-4-ylcarbonylamino)propanamide,

10) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(2-hydroxyethyl)thiazolidin-4-ylcarbonylamino)propanamide,

11) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(3-hydroxy-3-methylbutyl)thiazolidin-4-ylcarbonylamino)propanamide,

12) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(3-hydroxypropyl)thiazolidin-4-ylcarbonylamino)propanamide,

13) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-carboxymethylthiazolidin-4-ylcarbonylamino)propanamide,

14) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-t-butoxycarbonyl-1,1-dioxothiazolidin-4-ylcarbonylamino)propanamide,

15) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-t-butoxycarbonyl-1-oxothiazolidin-4-ylcarbonylamino)propanamide,

16) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((4S)-3-t-butoxycarbonyl-2-oxooxazolidin-4-ylcarbonylamino)propanamide,

17) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-hydroxymethylcarbonylthiazolidin-4-ylcarbonylamino)propanamide,

18) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(morpholin-4-ylcarbonylmethyl)thiazolidin-4-ylcarbonylamino)propanamide,

19) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(2-methoxyethoxycarbonyl)thiazolidin-4-ylcarbonylamino)propanamide,

20) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-chloromethoxycarbonylthiazolidin-4-ylcarbonylamino)propanamide,

21) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-(3,3-dimethylbutyryl)thiazolidin-4-ylcarbonylamino)propanamide,

22) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-cyclopentylcarbonylthiazolidin-4-ylcarbonylamino)propanamide,

23) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-benzoylthiazolidin-4-ylcarbonylamino)propanamide,

24) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((4R)-3-(3,3-dimethyl-1,2-dioxobutyl)thiazolidin-4-ylcarbonylamino)propanamide,

25) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((4R)-2,2,5,5-tetramethylthiazolidin-4-ylcarbonylamino)propanamide,

26) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((2S)-1-t-butoxycarbonyl-4-oxopyrrolidin-2-ylcarbonylamino)propanamide or

27) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-((2S, 4R)-1-t-butoxycarbonyl-4-hydroxypyrrolidin-2-ylcarbonylamino)propanamide

or non-toxic salts thereof.

11. (Original) A compound according to claim 1 which is

1) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-isopropylsulfonylthiazolidin-4-ylcarbonylamino)propanamide,

2) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-cyclopentylsulfonylthiazolidin-4-ylcarbonylamino)propanamide or

3) (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-isobutylsulfonylthiazolidin-4-ylcarbonylamino)propanamide

or non-toxic salts thereof.

12. (Previously Amended) A pharmaceutical composition comprising, as an active ingredient, an amino acid compound of the formula (I) depicted in claim 1, a non-toxic salt thereof, or a hydrate thereof, and a pharmaceutically acceptable carrier or diluent.

13.-15. (Canceled)

16. (Currently Amended) A method for treating ~~or preventing, or both,~~ a disease induced by an excessive release of neurotransmitters from N-type calcium channels, comprising administering to a host in need of such treatment an effective amount of an amino acid compound of formula (I) depicted in claim 1, a non-toxic salt thereof, or a hydrate thereof.

17. (Previously Presented) The method according to claim 16, wherein the disease induced by an excessive release of neurotransmitters from N-type calcium channels is selected from the group consisting of cerebral infarct, transient ischemic attack, encephalomyelopathy after cardiac operation, spinal angiopathy, hypertension with stress, neurosis, epilepsy, asthma and pollakiuria.

18. (Previously Presented) A method for the treatment of pain induced by an excessive release of neurotransmitters from N-type calcium channels, comprising administering to a host in need of such treatment an effective amount of an amino acid compound of formula (I) depicted in claim 1, a non-toxic salt thereof, or a hydrate thereof.